AMENDMENTS

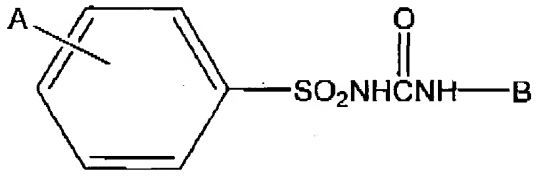
In the Claims

Please amend the claims as indicated below. A complete set of all claims previously submitted, including the status for each claim, immediately follows below.

1. (Original) A pharmaceutical composition comprising a pharmaceutically effective amount of at least one insulin secretagogue and a pharmaceutically effective amount of at least one FBPase inhibitor.

2. (Original) The pharmaceutical composition of claim 1 wherein said insulin secretagogue is a sulfonylurea antidiabetic agent.

3. (Original) The pharmaceutical composition of claim 2 wherein said sulfonylurea antidiabetic agent is a compound of formula XV:



(XV)

wherein

A is selected from hydrogen, halo, alkyl, alkanoyl, aryl, aralkyl, heteroaryl, and cycloalkyl; and

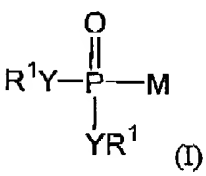
B is selected from alkyl, cycloalkyl, and heterocyclic alkyl.

4. (Original) The pharmaceutical composition of claim 2 wherein said sulfonylurea antidiabetic agent is selected from glyburide, glisoxepid, acetohexamide, chlorpropamide, glibornuride, tolbutamide, tolazamide, glipizide, gliclazide, gliquidone, glyhexamide, phenbutamide, tolcyclamide, and glimepiride.

5. (Original) The pharmaceutical composition of claim 1 wherein said insulin secretagogue is a non-sulfonylurea.

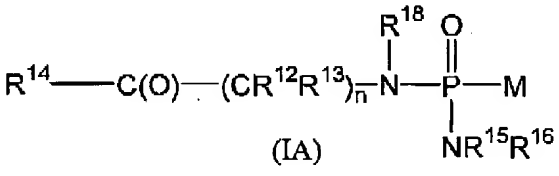
6. – 10. (Withdrawn)

11. (Original) The pharmaceutical composition of claim 1 wherein said FBPase inhibitor is a compound selected from formulae I and IA and pharmaceutically acceptable prodrugs and salts thereof, wherein formulae I and IA are as follows:



(I)

and



(IA)

wherein *in vivo* or *in vitro* compounds of formulae I and IA are converted to $M\text{-}PO_3^{2-}$, which inhibits FBPase, and wherein:

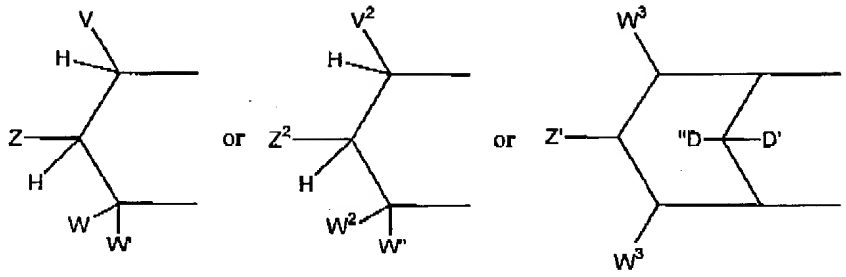
Y is independently selected from -O- and $-NR^6$, with the provisos that:

when Y is -O-, the R^1 attached to -O- is independently selected from -H, alkyl, optionally substituted aryl, optionally substituted alicyclic where the cyclic moiety contains a carbonate or a thiocarbonate, optionally substituted -arylalkyl, $-C(R^2)_2OC(O)NR^2_2$, $-NR^2\text{-}C(O)\text{-}R^3$, $-C(R^2)_2\text{-}OC(O)R^3$, $-C(R^2)_2\text{-}O\text{-}C(O)OR^3$, $-C(R^2)_2OC(O)SR^3$, -alkyl-S-C(O)R^3, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy;

when Y is $-NR^6$-, the R^1 attached to $-NR^6$- is independently selected from -H, $-[C(R^2)_2]_q\text{-}COOR^3$, $-C(R^4)_2COOR^3$, $-[C(R^2)_2]_q\text{-}C(O)SR$, and -cycloalkylene-$COOR^3$, where q is 1 or 2;

when only one Y is -O-, which -O- is not part of a cyclic group containing the other Y, the other Y is $-N(R^{18})\text{-}(CR^{12}R^{13})\text{-}C(O)\text{-}R^{14}$; and

when Y is independently selected from -O- and $-NR^6$, together R^1 and R^1 are alkyl-S-S-alkyl- and form a cyclic group, or together, R^1 and R^1 form :



wherein

a) V is selected from the group of aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkynyl and 1-alkenyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, said cyclic group is fused to an aryl group at the beta and gamma position to the Y adjacent to V; or

Z is selected from the group of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2$NHaryl, $-(CH_2)_p-OR^2$, and $-(CH_2)_p-SR^2$, where p is an integer 2 or 3; or

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl; or

W and W' are independently selected from the group of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl and 1-alkynyl; or

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

b) V^2, W^2 and W'' are independently selected from the group of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl;

Z^2 is selected from the group of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OCO_2R^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OC(S)OR^3$, -CH(aryl)OH, $-CH(CH{=}CR^2{}_2)OH$, $-CH(C{\equiv}CR^2)OH$, $-SR^2$, $-CH_2NHaryl$, $-CH_2aryl$; or

together V^2 and Z^2 are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 ring atoms, optionally containing 1 heteroatom, and substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from a Y attached to phosphorus;

c) Z' is selected from the group of -OH, $-OC(O)R^3$, $-OCO_2R^3$, and $-OC(O)SR^3$;

D' is –H;

D'' is selected from the group of -H, alkyl, $-OR^2$, -OH, and $-OC(O)R^3$;

each W^3 is independently selected from the group of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl;

with the proviso that:

a) V, Z, W, W' are not all –H and V^2, Z^2, W^2, W'' are not all –H ; and

R^2 is selected from R^3 and -H;

R^3 is selected from alkyl, aryl, alicyclic, and aralkyl;

each R^4 is independently selected from the group of -H, alkylene, -alkylenearyl and aryl, or together R^4 and R^4 are connected via 2-6 atoms, optionally including one heteroatom selected from the group of O, N, and S;

R^6 is selected from -H, lower alkyl, acyloxyalkyl, alkoxycarbonyloxyalkyl, and lower acyl;

n is an integer from 1 to 3;

R^{18} is independently selected from H, lower alkyl, aryl, and aralkyl, or, together, R^{12} and R^{18} are connected via 1-4 carbon atoms to form a cyclic group;

each R^{12} and each R^{13} is independently selected from H, lower alkyl, lower aryl, lower aralkyl, all optionally substituted, or R^{12} and R^{13}, together, are connected via 2-6 carbon atoms, optionally including 1 heteroatom selected from the group of O, N, and S, to form a cyclic group;

each R^{14} is independently selected from $-OR^{17}$, $-N(R^{17})_2$, $-NHR^{17}$, $-SR^{17}$, and $-NR^2R^{20}$;

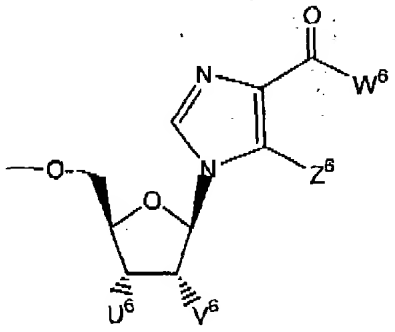
R^{15} is selected from -H, lower alkyl, lower aryl, and lower aralkyl, or, together, R^{15} and R^{16} are connected via 2-6 atoms to form a cyclic group, wherein the cyclic group optionally includes one heteroatom selected from O, N, and S;

R^{16} is selected from $-(CR^{12}R^{13})_n-C(O)-R^{14}$, -H, lower alkyl, lower aryl, and lower aralkyl, or, together, R^{15} and R^{16} are connected via 2-6 atoms to form a cyclic group, wherein the cyclic group optionally includes one heteroatom selected from O, N, and S;

each R^{17} is independently selected from lower alkyl, lower aryl, and lower aralkyl, or, when R^{14} is $-N(R^{17})_2$, together, both R^{17}s are connected via 2-6 atoms to form a cyclic group, wherein the cyclic group optionally includes one heteroatom selected from O, N, and S;

R^{20} is selected from the group of –H, lower R^3, and –C(O)-lower R^3.

12. (Original) The pharmaceutical composition of claim 11 wherein M is:



wherein:

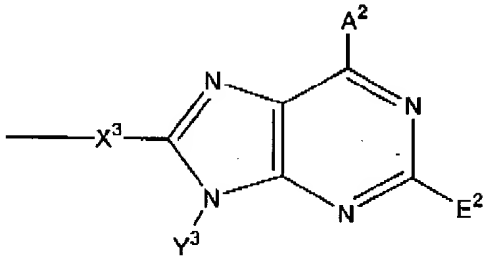
U^6 and V^6 are independently selected from hydrogen, hydroxy, and acyloxy, or, when taken together, U^6 and V^6 form a lower cyclic ring containing at least one oxygen;

W^6 is selected from amino and lower alkyl amino; and

Z^6 is selected from alkyl and halogen.

13. (Original) The pharmaceutical composition of claim 11 wherein said insulin secretagogue is a sulfonylurea antidiabetic agent.

14. (Original) The pharmaceutical composition of claim 11 wherein M is:



wherein:

A^2 is selected from $-NR^8_2$, $-NHSO_2R^3$, $-OR^{25}$, $-SR^{25}$, halogen, lower alkyl, $-CON(R^4)_2$, guanidine, amidine, -H, and perhaloalkyl;

E^2 is selected from -H, halogen, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, -CN, and $-NR^7_2$;

X^3 is selected from -alkyl(hydroxy)-; -alkyl-; -alkynyl-; -aryl-; -carbonyl-alkyl-; -1,1-dihaloalkyl-; -alkoxyalkyl-; -alkyloxy-; -alkylthioalkyl-; -alkylthio-; -alkylaminocarbonyl-; -alkylcarbonylamino-; -alicyclic-; -aralkyl-; -alkylaryl-; -alkoxycarbonyl-; -carbonyloxyalkyl-; -alkoxycarbonylamino-; and -alkylaminocarbonylamino-, all optionally substituted, with the proviso that X^3 is not substituted with $-COOR^2$, $-SO_3H$, or $-PO_3R^2_2$;

Y^3 is selected from -H, alkyl, alkenyl, alkynyl, aryl, alicyclic, aralkyl, aryloxyalkyl, alkoxyalkyl, $-C(O)R^3$, $-S(O)_2R^3$, $-C(O)-R^{11}$, $-CONHR^3$, $-NR^2_2$, and $-OR^3$, all, except H, optionally substituted;

each R^4 is independently selected from –H and alkyl, or, together, both R^4s form a cyclic alkyl group;

R^{25} is selected from lower alkyl, lower aryl, lower aralkyl, and lower alicyclic;

each R^7 is independently selected from -H, lower alkyl, lower alicyclic, lower aralkyl, lower aryl, and $-C(O)R^{10}$;

each R^8 is independently selected from -H, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, $-C(O)R^{10}$, or, together, both R^8s form a bidendate alkyl;

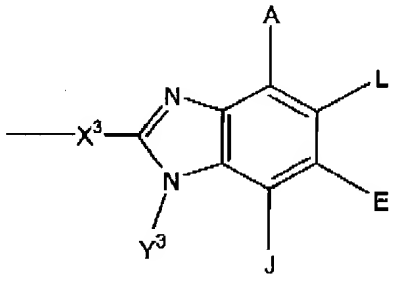
R^{10} is selected from -H, lower alkyl, $-NH_2$, lower aryl, and lower perhaloalkyl;

R^{11} is selected from alkyl, aryl, $-NR^2{}_2$, and $-OR^2$;

and pharmaceutically acceptable prodrugs and salts thereof.

15. (Original) The pharmaceutical composition of claim 14 wherein said insulin secretagogue is a sulfonylurea antidiabetic agent.

16. (Original) The pharmaceutical composition of claim 11 wherein M is:



wherein:

A, E, and L are independently selected from $-NR^8{}_2$, $-NO_2$, -H, $-OR^7$, $-SR^7$, $-C(O)NR^4{}_2$, halo, $-COR^{11}$, $-SO_2R^3$, guanidine, amidine, $-NHSO_2R^{25}$, $-SO_2NR^4{}_2$, -CN, sulfoxide, perhaloacyl, perhaloalkyl, perhaloalkoxy, C_1-C_5 alkyl, C_2-C_5 alkenyl, C_2-C_5 alkynyl, and lower alicyclic, or, together, A and L form a cyclic group, or, together, L and E form a cyclic group, or, together, E and J form a cyclic group selected from the group of aryl, cyclic alkyl, and heterocyclic;

J is selected from $-NR^8{}_2$, $-NO_2$, -H, $-OR^7$, $-SR^7$, $-C(O)NR^4{}_2$, halo,

-C(O)R^{11}, -CN, sulfonyl, sulfoxide, perhaloalkyl, hydroxyalkyl, perhaloalkoxy, alkyl, haloalkyl, aminoalkyl, alkenyl, alkynyl, alicyclic, aryl, and aralkyl, or, together, J and Y form a cyclic group selected from the group of aryl, cyclic alkyl, and heterocyclic alkyl;

X^3 is selected from -alkyl(hydroxy)-; -alkyl-; -alkynyl-; -aryl-; -carbonyl-alkyl-; -1,1-dihaloalkyl-; -alkoxyalkyl-; -alkyloxy-; -alkylthioalkyl-; -alkylthio-; -alkylaminocarbonyl-; -alkylcarbonylamino-; -alicyclic-; -aralkyl-; -alkylaryl-; -alkoxycarbonyl-; -carbonyloxyalkyl-; -alkoxycarbonylamino-; and -alkylaminocarbonylamino-, all optionally substituted, with the proviso that X^3 is not substituted with -$COOR^2$, -SO_3H, or -$PO_3R^2_2$;

Y^3 is selected from -H, alkyl, alkenyl, alkynyl, aryl, alicyclic, aralkyl, aryloxyalkyl, alkoxyalkyl, -C(O)R^3, -$S(O)_2R^3$, -C(O)-R^{11}, -$CONHR^3$, -NR^2_2, and -OR^3, all except H are optionally substituted;

each R^4 is independently selected from –H and alkyl, or, together, both R^4s form a cyclic alkyl group;

R^{25} is selected from lower alkyl, lower aryl, lower aralkyl, and lower alicyclic;

each R^7 is independently selected from -H, lower alkyl, lower alicyclic, lower aralkyl, lower aryl, and -C(O)R^{10};

each R^8 is independently selected from -H, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, -C(O)R^{10}, or, together, both R^8s form a bidendate alkyl;

R^{10} is selected from -H, lower alkyl, -NH_2, lower aryl, and lower perhaloalkyl; and

R^{11} is selected from alkyl, aryl, -NR^2_2, and -OR^2;

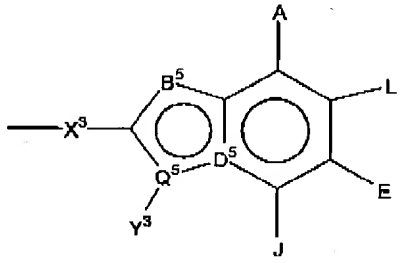
and pharmaceutically acceptable prodrugs and salts thereof.

17. (Original) The pharmaceutical composition of claim 16 wherein said insulin secretagogue is a sulfonylurea antidiabetic agent.

18. (Original) The pharmaceutical composition of claim 17 wherein said sulfonylurea antidiabetic agent is selected from glyburide, glisoxepid, acetohexamide, chlorpropamide, glibornuride, tolbutamide, tolazamide, glipizide, gliclazide, gliquidone, glyhexamide, phenbutamide, tolcyclamide, and glimepiride.

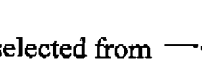
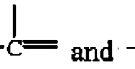
19. (Withdrawn)

20. (Original) The pharmaceutical composition of claim 11 wherein M is:



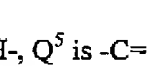
wherein:

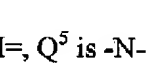
B^5 is selected from -NH-, -N= and -CH=;

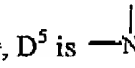
D^5 is selected from  and  ;

Q^5 is selected from -C= and -N-;

with the provisos that:

when B^5 is -NH-, Q^5 is -C= and D^5 is  ;

when B^5 is -CH=, Q^5 is -N- and D^5 is  ; and

when B^5 is -N=, D^5 is  and Q^5 is -C=;

A, E, and L are independently selected from $-NR^8_2$, $-NO_2$, -H, $-OR^7$, $-SR^7$, $-C(O)NR^4_2$, halo, $-COR^{11}$, $-SO_2R^3$, guanidine, amidine, $-NHSO_2R^{25}$, $-SO_2NR^4_2$, -CN, sulfoxide, perhaloacyl, perhaloalkyl, perhaloalkoxy, C_1-C_5 alkyl, C_2-C_5 alkenyl, C_2-C_5 alkynyl, and lower alicyclic, or, together, A and L form a cyclic group, or, together, L and E form a cyclic group, or, together, E and J form a cyclic group selected from the group of aryl, cyclic alkyl, and heterocyclic;

J is selected from $-NR^8_2$, $-NO_2$, -H, $-OR^7$, $-SR^7$, $-C(O)NR^4_2$, halo, $-C(O)R^{11}$,

-CN, sulfonyl, sulfoxide, perhaloalkyl, hydroxyalkyl, perhaloalkoxy, alkyl, haloalkyl, aminoalkyl, alkenyl, alkynyl, alicyclic, aryl, and aralkyl, or together with Y forms a cyclic group selected from the group of aryl, cyclic alkyl and heterocyclic alkyl;

X^3 is selected from -alkyl(hydroxy)-, -alkyl-, -alkynyl-, -aryl-, -carbonyl-alkyl-, -1,1-dihaloalkyl-, -alkoxyalkyl-, -alkyloxy-, -alkylthioalkyl-, -alkylthio-, -alkylaminocarbonyl-, -alkylcarbonylamino-, -alicyclic-, -aralkyl-, -alkylaryl-, -alkoxycarbonyl-, -carbonyloxyalkyl-, -alkoxycarbonylamino-, and -alkylaminocarbonylamino-, all optionally substituted; with the proviso that X^3 is not substituted with $-COOR^2$, $-SO_3H$, or $-PO_3R^2_2$;

Y^3 is selected from -H, alkyl, alkenyl, alkynyl, aryl, alicyclic, aralkyl, aryloxyalkyl, alkoxyalkyl, $-C(O)R^3$, $-S(O)_2R^3$, $-C(O)-R^{11}$, $-CONHR^3$, $-NR^2_2$, and $-OR^3$, all except H are optionally substituted;

R^4 is independently selected from -H and alkyl, or together R^4 and R^4 form a cyclic alkyl group;

R^{25} is selected from lower alkyl, lower aryl, lower aralkyl, and lower alicyclic;

R^7 is independently selected from -H, lower alkyl, lower alicyclic, lower aralkyl, lower aryl, and $-C(O)R^{10}$;

R^8 is independently selected from -H, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, $-C(O)R^{10}$, or together they form a bidentate alkyl;

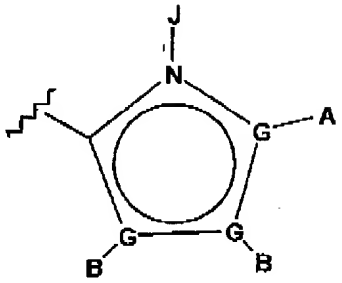
R^{10} is selected from -H, lower alkyl, $-NH_2$, lower aryl, and lower perhaloalkyl;

R^{11} is selected from alkyl, aryl, $-NR^2_2$ and $-OR^3$;

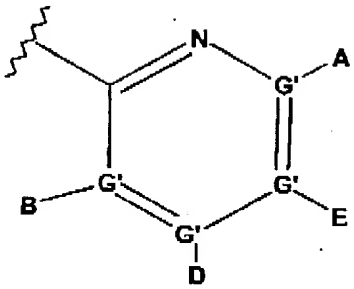
and pharmaceutically acceptable prodrugs and salts thereof.

21. (Original) The pharmaceutical composition of claim 20 wherein said insulin secretagogue is a sulfonylurea antidiabetic agent.

22. (Original) The pharmaceutical composition of claim 11 wherein M is $-X-R^5$ wherein R^5 is selected from:



and



wherein:

each G is independently selected from C, N, O, S, and Se, and wherein not more than one G is O, S, or Se, and not more than one G is N;

each G' is independently selected from C and N and wherein no more than two G' groups are N;

A is selected from -H, $-NR^4_2$, $-CONR^4_2$, $-CO_2R^3$, halo, $-S(O)R^3$, $-SO_2R^3$, alkyl, alkenyl, alkynyl, perhaloalkyl, haloalkyl, aryl, $-CH_2OH$, $-CH_2NR^4_2$, $-CH_2CN$, -CN, $-C(S)NH_2$, $-OR^3$, $-SR^3$, $-N_3$, $-NHC(S)NR^4_2$, -NHAc, and null;

each B and D are independently selected from -H, alkyl, alkenyl, alkynyl, aryl, alicyclic, aralkyl, alkoxyalkyl, $-C(O)R^{11}$, $-C(O)SR^3$, $-SO_2R^{11}$, $-S(O)R^3$, -CN, $-NR^9_2$, $-OR^3$, $-SR^3$, perhaloalkyl, halo, $-NO_2$, and null, all except -H, -CN, perhaloalkyl, $-NO_2$, and halo are optionally substituted;

E is selected from -H, alkyl, alkenyl, alkynyl, aryl, alicyclic, alkoxyalkyl, $-C(O)OR^3$, $-CONR^4_2$, -CN, $-NR^9_2$, $-NO_2$, $-OR^3$, $-SR^3$, perhaloalkyl, halo, and null, all except -H, -CN, perhaloalkyl, and halo are optionally substituted;

J is selected from -H and null;

X is an optionally substituted linking group that links R^5 to the phosphorus atom via 2-4 atoms, including 0-1 heteroatoms selected from N, O, and S, except that if X is urea or carbamate there are 2 heteroatoms, measured by the shortest path between R^5 and the phosphorus atom, and wherein the atom attached to the phosphorus is a carbon atom, and wherein X is selected from furan-2,5-diyl, -alkyl(hydroxy)-, -alkynyl-, -heteroaryl-, -carbonylalkyl-, -1,1-dihaloalkyl-, -alkoxyalkyl-, -alkyloxy-, -alkylthioalkyl-, -alkyl-thio-, -alkylaminocarbonyl-, -alkylcarbonylamino-, -alkoxycarbonyl-, -carbonyloxyalkyl-,

-alkoxycarbonylamino-, and -alkylaminocarbonylamino-, all optionally substituted; with the proviso that X is not substituted with $-COOR^2$, $-SO_3H$, or $-PO_3R^2_2$;

R^2 is selected from R^3 and -H;

R^3 is selected from alkyl, aryl, alicyclic, and aralkyl;

each R^4 is independently selected from -H, and alkyl, or together R^4 and R^4 form a cyclic alkyl group;

each R^9 is independently selected from -H, alkyl, aralkyl, and alicyclic, or together R^9 and R^9 form a cyclic alkyl group or a heterocyclic group where the heteroatom is selected from the group of O,S and N;

R^{11} is selected from alkyl, aryl, $-NR^2_2$, and $-OR^2$;

and with the proviso that:

1) when G' is N, then the respective A, B, D, or E is null;

2) at least one of A and B, or A, B, D, and E is not selected from -H or null;

3) when R^5 is a six-membered ring, then X is not any 2 atom linker, an optionally substituted -alkyloxy-, or an optionally substituted -alkylthio-;

4) when G is N, then the respective A or B is not halogen or a group directly bonded to G via a heteroatom;

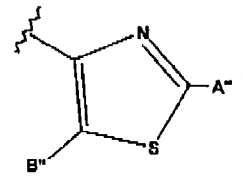
5) when X is not an -aryl- group, then R^5 is not substituted with two or more aryl groups;

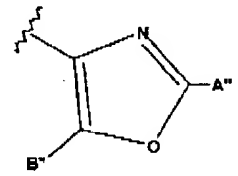
and pharmaceutically acceptable prodrugs and salts thereof.

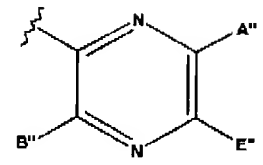
23. (Original) The pharmaceutical compositions of claim 22 wherein R^5 is selected from pyrrolyl; imidazolyl; oxazolyl; thiazolyl; isothiazolyl; 1,2,4-thiadiazolyl; pyrazolyl; isoxazolyl; 1,2,3-oxadiazolyl; 1,2,4-oxadiazolyl; 1,2,5-oxadiazolyl; 1,3,4-oxadiazolyl; 1,2,4-thiadiazolyl; 1,3,4-thiadiazolyl; pyridinyl; pyrimidinyl; pyrazinyl; pyridazinyl; 1,3,5-triazinyl; 1,2,4-triazinyl; and 1,3-selenazolyl, all of which contain at least one substituent.

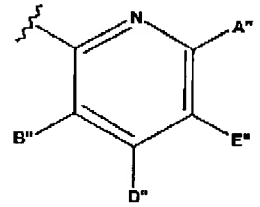
24. (Original) The pharmaceutical composition of claim 22 wherein R^5 is not 2-thiazolyl or 2-oxazolyl.

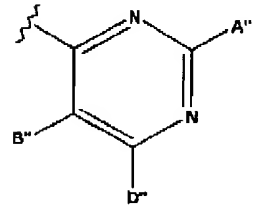
25. (Original) The pharmaceutical composition of claim 22 wherein R^5 is selected from the group of:











wherein:

A" is selected from -H, $-NR^4_2$, $-CONR^4_2$, $-CO_2R^3$, halo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 perhaloalkyl, C_1-C_6 haloalkyl, aryl, $-CH_2OH$, $-CH_2NR^4_2$, $-CH_2CN$, -CN, $-C(S)NH_2$, $-OR^3$, $-SR^3$, $-N_3$, $-NHC(S)NR^4_2$, and -NHAc;

B" and D" are independently selected from -H, alkyl, alkenyl, alkynyl, aryl, alicyclic, aralkyl, alkoxyalkyl, $-C(O)R^{11}$, $-C(O)SR^3$, $-SO_2R^{11}$, $-S(O)R^3$, -CN, $-NR^9_2$, $-OR^3$, $-SR^3$, perhaloalkyl, and halo, all except -H, -CN, perhaloalkyl, and halo are optionally substituted;

E" is selected from -H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_4-C_6 alicyclic, alkoxyalkyl, -C(O)OR^3, -$CONR^4_2$, -CN, -NR^9_2, -OR^3, -SR^3, C_1-C_6 perhaloalkyl, and halo, all except H, -CN, perhaloalkyl, and halo are optionally substituted; and

each R^3 is independently selected from C_1–C_6 alkyl, C_6 aryl, C_3–C_6 heteroaryl, C_3–C_8 alicyclic, C_2–C_7 heteroalicyclic, C_7–C_{10} aralkyl, and C_4–C_9 heteroaralkyl;

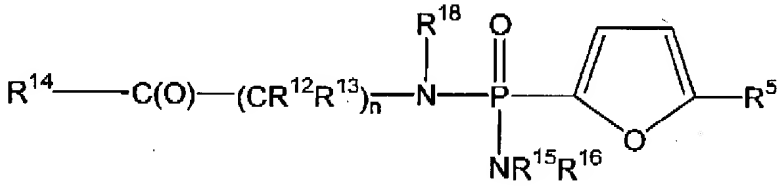
each R^4 and R^9 is independently selected from -H and C_1-C_2 alkyl;

X is selected from -heteroaryl-, -alkylcarbonylamino-, -alkylaminocarbonyl-, and -alkoxycarbonyl-;

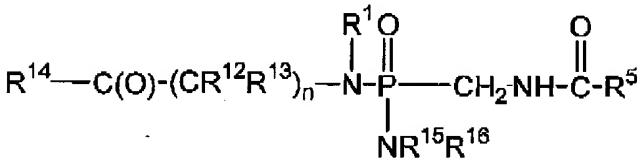
each R^{11} is selected from -NR^4_2, -OH, -OR^3, C_1–C_6 alkyl, C_6 aryl, and C_3–C_6 heteroaryl.

26. (Original) The pharmaceutical composition of claim 25 wherein X is selected from -heteroaryl- and -alkoxycarbonyl-.

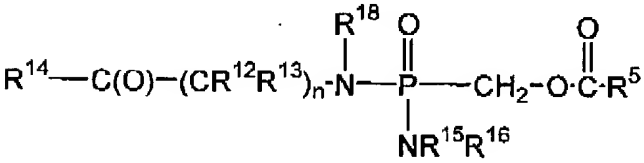
27. (Original) The pharmaceutical composition of claim 25 wherein said compound is a compound of formulae XII, XIII, or XIV:



(XII)



(XIII)



(XIV).

28. (Original) The pharmaceutical composition of claim 25 wherein:

A" is selected from $-NH_2$, -Cl, -Br, and $-CH_3$;

each B" is selected from -H, $-C(O)OR^3$, $-C(O)SR^3$, C1-C6 alkyl, alicyclic, halo, heteroaryl, and $-SR^3$;

D" is selected from -H, $-C(O)OR^3$, lower alkyl, alicyclic, and halo; and

E" is selected from -H, -Br, and -Cl.

29. (Original) The pharmaceutical composition of claim 27 wherein:

R^{18} is selected from -H, methyl, and ethyl;

each R^{12} and R^{13} is independently selected from -H, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, $-CH_2CH_2-SCH_3$, phenyl, and benzyl, or together R^{12} and R^{13} are connected via a chain of 2-5 carbon atoms to form a cycloalkyl group;

n is 1 or 2;

each R^{14} is independently selected from $-OR^{17}$, wherein R^{17} is selected from methyl, ethyl, propyl, and benzyl; and

R^{15} and R^{16} are independently selected from lower alkyl and lower aralkyl, or together R^{15} and R^{16} are connected via a chain of 2-6 atoms, optionally including 1 heteroatom selected from O, N, and S.

30. (Original) The pharmaceutical composition of claim 27 wherein R^{16} is $-(CR^{12}R^{13})_n-C(O)-R^{14}$.

31. (Original) The pharmaceutical composition of claim 27 wherein:

R^{18} is selected from -H, methyl, and ethyl;

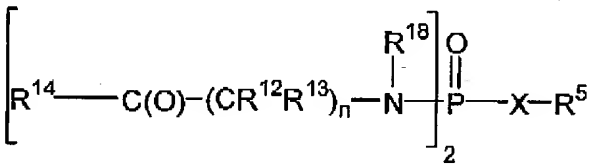
R^{12} and R^{13} are independently selected from -H, methyl, i-propyl, i-butyl, and benzyl, or together are connected via a chain of 2-5 carbon atoms to form a cycloalkyl group;

R^{14} is $-OR^{17}$;

R^{17} is selected from methyl, ethyl, propyl, t-butyl, and benzyl; and

R^{15} and R^{16} are independently selected from lower alkyl, and lower aralkyl, or together R^{15} and R^{16} are connected via a chain of 2-6 atoms, optionally including 1 heteroatom selected from O, and N.

32. (Original) The pharmaceutical composition of claim 22 wherein said FBPase inhibitor is a compound of the formula:



wherein X is selected from furan-2,5-diyl; -alkoxycarbonyl-; and -alkylaminocarbonyl-.

33. (Original) The pharmaceutical composition of claim 32 wherein:

n is 1;

R^{12} and R^{13} are independently selected from -H, methyl, i-propyl, i-butyl, and benzyl, or, together, R^{12} and R^{13} are connected via a chain of 2-5 carbon atoms to form a cycloalkyl group, and, when R^{12} and R^{13} are not the same, H_2N-$CR^{12}R^{13}$-C(O)-R^{14} is an ester or thioester of a naturally occurring amino acid;

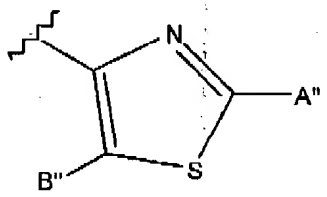
R^{14} is selected from -OR^{17} and -SR^{17};

R^{17} is selected from methyl, ethyl, propyl, t-butyl, and benzyl; and

R^{18} is selected from -H, methyl, and ethyl.

34. (Original) The pharmaceutical composition of claim 25 wherein:

R^5 is:

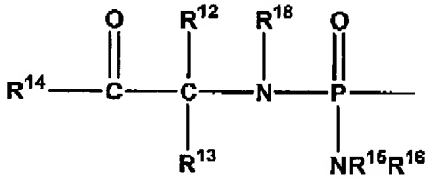


A" is selected from -NH_2, -$CONH_2$, halo, -CH_3, -CF_3, -CH_2-halo, -CN, -OCH_3, -SCH_3, and -H;

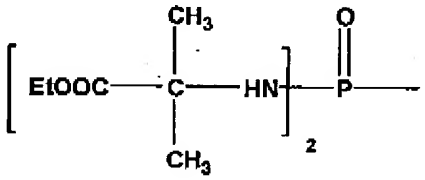
B" is selected from -H, -C(O)R^{11}, -C(O)SR^3, alkyl, aryl, alicyclic, halo, -CN, -SR^3, OR^3, and -$NR^9{}_2$; and

X is selected from -heteroaryl-, -alkoxycarbonyl-, and -alkylaminocarbonyl-, all optionally substituted.

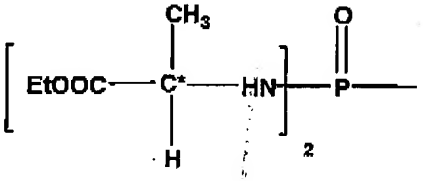
35. (Original) The pharmaceutical compositions of claim 34 wherein said FBPase inhibitor is a compound of Formula 1A and wherein:



is selected from



and



wherein:

C* has S stereochemistry;

R^{18} and R^{15} are independently selected from H and methyl;

each R^{12} and R^{13} is independently selected from -H, methyl, i-propyl, i-butyl, and benzyl, or together R^{12} and R^{13} are connected via a chain of 2-5 carbon atoms to form a cycloalkyl group;

n is 1;

R^{14} is -OR^{17};

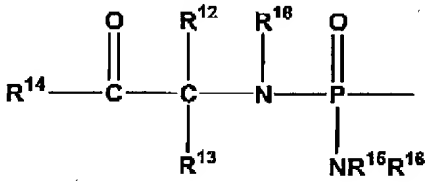
R^{16} is $-(CR^{12}R^{13})_n-C(O)-R^{14}$; and

R^{17} is selected from methyl, ethyl, propyl, phenyl, and benzyl.

36. (Original) The pharmaceutical composition of claim 34 wherein A" is $-NH_2$, X is furan-2,5-diyl, and B" is $-S(CH_2)_2CH_3$.

37. (Original) The pharmaceutical composition of claim 34 wherein A" is $-NH_2$, X is furan-2,5-diyl, and B" is $-CH_2-CH(CH_3)_2$.

38. (Original) The pharmaceutical composition of claim 37 wherein said FBPase inhibitor is a compound of Formula 1A and wherein



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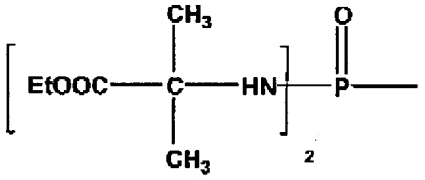
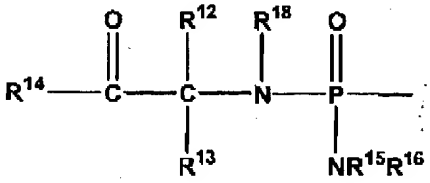
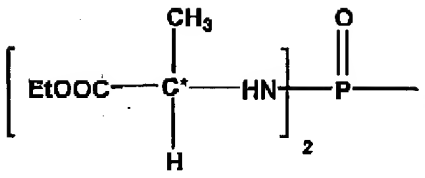


39. (Original) The pharmaceutical composition of claim 37 wherein said FBPase inhibitor is a compound of Formula 1A and wherein



is



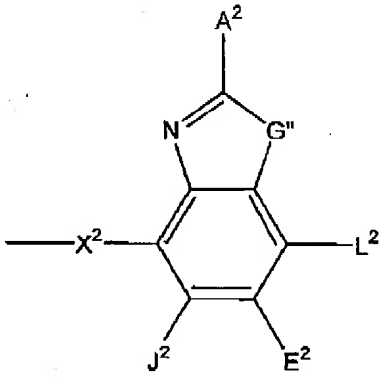
wherein C* has S stereochemistry.

40. (Original) The pharmaceutical composition of claim 22 wherein said insulin secretagogue is a sulfonylurea antidiabetic agent.

41. (Original) The pharmaceutical composition of claim 40 wherein said sulfonylurea antidiabetic agent is selected from glyburide, glisoxepid, acetohexamide, chlorpropamide, glibornuride, tolbutamide, tolazamide, glipizide, gliclazide, gliquidone, glyhexamide, phenbutamide, tolcyclamide, and glimepiride.

42. (Original) The pharmaceutical composition of claim 22 wherein said insulin secretagogue is selected from mitiglinide, BTS-67582, repaglinide, nateglinide, dipeptidyl peptidase-IV (DPP-IV) inhibitors, and glucagon like peptide-1 (GLP-1) receptor agonists.

43. (Original) The pharmaceutical composition of claim 11 wherein M is



wherein:

G" is selected from -O- and -S-;

A^2, L^2, E^2, and J^2 are selected from $-NR^4_2$, $-NO_2$, -H, $-OR^2$, $-SR^2$, $-C(O)NR^4_2$, halo, $-COR^{11}$, $-SO_2R^3$, guanidinyl, amidinyl, aryl, aralkyl, alkoxyalkyl, -SCN, $-NHSO_2R^9$, $-SO_2NR^4_2$, -CN, $-S(O)R^3$, perhaloacyl, perhaloalkyl, perhaloalkoxy, C_1-C_5 alkyl, C_2-C_5 alkenyl, C_2-C_5 alkynyl, and lower alicyclic, or together L^2 and E^2 or E^2 and J^2 form an annulated cyclic group;

X^2 is selected from $-CR^2_2$-, $-CF_2$-, $-CR^2_2$-O-, $-CR^2_2$-S-, -C(O)-O-, -C(O)-S-, –C(S)-O-, and $-CR^2_2-NR^{19}$-, and wherein in the atom attached to the phosphorus is a carbon atom; with the proviso that X^2 is not substituted with $-COOR^2$, $-SO_3H$, or $-PO_3R^2_2$;

R^2 is selected from R^3 and -H;

R^3 is selected from alkyl, aryl, alicyclic, and aralkyl;

each R^4 is independently selected from -H, and alkyl, or together R^4 and R^4 form a cyclic alkyl group;

each R^9 is independently selected from -H, alkyl, aralkyl, and alicyclic, or together R^9 and R^9 form a cyclic alkyl group;

R^{11} is selected from alkyl, aryl, $-NR^2_2$, and $-OR^2$;

R^{19} is selected from lower alkyl, -H, and $-COR^2$;

and pharmaceutically acceptable prodrugs and salts thereof.

44. (Original) The pharmaceutical composition of claim 43 wherein G" is -S-.

45. (Original) The pharmaceutical composition of claim 43 wherein said insulin secretagogue is a sulfonylurea antidiabetic agent.

46. –114. (Withdrawn)